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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,193	05/29/2001	Christopher C. Adams	GP100-03.CN1	7798

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	15

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/867,193	Adams
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 7, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18 and 34-39* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18 and 34-39* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-16 and 36-39 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wright et al. (Science, (25 April, 1997), Vol. 26, pages 614-617) in view of Kacian et al. (U.S. Patent 5,554,516) (September 10, 1996).

Wright et al teach a purified decoy probe (Abstract and page 616, column 2, lines 6-10) comprising,

a first nucleotide base recognition sequence region, wherein the first region binds to an RNA polymerase (Figure 1 and page 615, column 1, second paragraph, lines 1-18)., and

the first region is nucleic acid which can be used to produce a functional double-stranded promoter sequence using a complementary oligonucleotide wherein the first region does not have a nucleic acid sequence greater than about 10 nucleotides in length joined directly to the 3' end of the first region (Page 615, column 3, second paragraph, lines 1-6).

Wright et al further teach the probe wherein the RNA polymerase is T7 RNA polymerase and other bacteriophage RNA polymerases (Page 615, column 1, first paragraph to column 3, second paragraph).

Wright et al further teach the probe wherein the first region has at least 35 % sequence similarity to an RNA polymerase promoter sequence (Page 615, column 3, second paragraph, lines 1 to page 616, column 1, line 4).

Wright et al further teach a reaction mixture for use in amplification reaction comprising a nucleic acid polymerase and nucleotides having a similarity to an RNA polymerase promoter sequence.

Wright et al do not teach an optionally present second nucleotide base recognition sequence region provided that the second region is either directly joined to the 5' end of the first region or is joined to the 3' end or 5' end of the first region by a non-nucleotide phosphorothioate linker.

Kacian et al teach an optionally present second nucleotide base recognition sequence region provided that the second region is either directly joined to the 5' end of the first region or is joined to the 3' end or 5' end of the first region by a non-nucleotide phosphorothioate linker (Figures 1-2 and Column 6, line 54 to Column 7, line 23 and Column 8, line 55 to Column 9, line 32 and Claim 21).

Kacian et al further teach the probe wherein at least 80 % of the modified nucleosides have a purine or pyrimidine moiety independently selected from adenine, guanine and thymine and at least 80 % of the internucleoside linkages joining the optionally modified nucleosides are phosphodiester (Figure 3 and Claim 28).

Wright et al do not teach a probe that does not have a terminal 3' OH group available to accept a nucleoside triphosphate in a polymerization reaction.

Kacian et al further teach the probe wherein the probe consists 15 to 100 independently selected deoxyribonucleotides and one or more blocking groups located at the 3' terminus of the probe which is a probe that does not have a terminal 3' OH group available to accept a nucleoside triphosphate in a polymerization reaction (Column 8, line 55 to Column 9, line 32 and Claim 21).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize, within the method of Wright et al., the modified, high affinity oligonucleotide ligands of Kacian et al. since Kacian et al state, "The 3'-end of the primer or promoter-primer may be modified, or blocked, so as to prohibit or inhibit an extension reaction from proceeding therefrom (Column 8, lines 57-59)". An ordinary artisan would have been

motivated by the express statement of Kacian et al. to combine and utilize, within the method of Wright et al., the modified, high affinity oligonucleotide ligands of Kacian et al. in order to achieve the express advantages, as noted by Kacian et al. of the 3'-end of the primer or promoter-primer that may be modified, or blocked, so as to prohibit or inhibit an extension reaction from proceeding therefrom.

3. Claims 17 and 18 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wright et al. (Science, (25 April, 1997), Vol. 26, pages 614-617) in view of Kacian et al. (U.S. Patent 5,554,516) (September 10, 1996) further in view of Olson et al. (U.S. Patent 5,861,273) (January 19, 1999).

Wright et al. in view of Kacian et al teach the probe of claims 1-16 as described above.

Wright et al. in view of Kacian et al do not teach the probe wherein the first region has a nucleotide base sequence similarity of at least 75 % with at least one of SEQ ID Nos. 1-6.

Olson et al teach the probe wherein the first region has a nucleotide base sequence similarity of 100 % with SEQ ID No. 3 (Sequence No: 4, column 37).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize, within the method of Wright et al in view of Kacian et al., the specific nucleotide base sequence of Olson et al. since Olson et al state, "The present invention, therefore, provides a method for producing a heterologous protein of interest (Column 3, lines 47-48)". An ordinary artisan would have been motivated by the express statement of Olson et al. to combine and utilize, within the method of Wright et al in view of Kacian et al., the specific

nucleotide base sequence of Olson et al. in order to achieve the express advantages, as noted by Olson et al. of a nucleotide system which provides a method for producing a heterologous protein of interest.

4. Claims 34-35 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wright et al. (Science, (25 April, 1997), Vol. 26, pages 614-617) in view of Kacian et al. (U.S. Patent 5,554,516) (September 10, 1996) further in view of Dattagupta (U.S. Patent 5,215,899) (June 1, 1993).

Wright et al. in view of Kacian et al teach the probe of claims 1-16 as described above.

Wright et al. in view of Kacian et al do not teach the purified decoy probe containing a region of self-complementarity.

Dattagupta teaches the purified decoy probe containing a region of self-complementarity (Abstract and Figures 1-4 and Examples 1-3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the purified decoy probe containing a region of self-complementarity of Dattagupta in the method of Wright et al in view of Kacian et al., since Dattagupta states, " Specific nucleic acid sequences are amplified through the use of a hairpin probe which, upon hybridization with and ligation to a target sequence is capable of being transcribed. The probe comprises a single stranded self-complementary sequence which, under hybridizing conditions, forms a hairpin structure having a functional promoter region, and further comprises a single stranded probe sequence extending from the 3' end of the hairpin sequence.

Upon hybridization with a target sequence complementary to the probe sequence and ligation of the 3' end of the hybridized target sequence to the 5' end of the hairpin probe, the target sequence is rendered transcribable in the presence of a suitable RNA polymerase and appropriate rNTPs. Amplification is accomplished by hybridizing the desired target nucleic acid sequence with the probe, ligating the target sequence to the probe, adding the RNA polymerase and rNTPs to the separated hybrids, and allowing transcription to proceed until a desired amount of RNA transcription product has accumulated. The amplification method is particularly useful in assays for the detection of particular nucleic acid sequences (Abstract)". An ordinary artisan would have been motivated by the express statement of Dattagupta to substitute and combine the purified decoy probe containing a region of self-complementarity of Dattagupta in the method of Wright et al in view of Kacian et al. in order to achieve the express advantages, as noted by Dattagupta, of self complementary probes and amplification method which are particularly useful in assays for the detection of particular nucleic acid sequences and the target sequence is rendered transcribable in the presence of a suitable RNA polymerase and appropriate rNTPs allowing transcription to proceed until a desired amount of RNA transcription product has accumulated.

Response to Arguments

5. Applicant's arguments filed on November 7, 2002 have been fully considered but they are not persuasive.

Applicant argues that none of the references teaches the non-nucleotide linker between a primer and a promoter of RNA polymerase. Applicant is hereby notified that it is not an absolute

requirement of the claims that such linker has to be present in the cited references because the presence of second nucleotide sequence (primer) is an option, not an absolute requirement.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Kacian reference does not teach the linking of the promoter and primer with a phosphorothioate of the claimed invention. Applicant argues that the word "linking of the promoter and primer with a phosphorothioate" was not found in Kacian reference. Applicant argues that because Kacian has a preferred embodiment of hybridization of promoter-primer sequence with target sequence, Kacian is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Kacian has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Kacian reference uses hybridization or promoter-primer with target sequences to amplify the

nucleotides, the property of non-nucleotide linker between promoter and primer is inherently present in this chemically and structurally identical molecule. For example, Kacian teaches, "The results showed that promoter-primers with one or two ribonucleotides at the 3' end, or with a 3' phsphorothioate linkage, gives better amplification in this system than unmodified promoter-primers (Example 9, Column 15, lines 43-46). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)".

Applicant argues that 3' phsphothioate linkage is different than non-nucleotide linkers. Applicant's argument is not persuasive. In this case, 3' phsphothioate linkage can be considered as the species of the genus non-nucleotide linker.

In view of the response to argument, all previous 103(a) rejections have been maintained properly.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

November 26, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600